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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER

DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 05/21/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/438,185

Applicant(s)

Stephens et al

Examiner

Duffy

Group Art Unit

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—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 3-13-02
- ☒ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 11-22 is/are pending in the application.
- Of the above claim(s) 11-16 is/are withdrawn from consideration.
- ☐ Claim(s) is/are allowed.
- ☒ Claim(s) 17-22 is/are rejected.
- ☐ Claim(s) is/are objected to.
- ☒ Claim(s) 11-22 are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

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Response to Amendment

1. The amendment filed 3-13-02 has been entered into the record. Claims 1-10 have been canceled, new claims 11-22 have been added.
2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restriction

3. Newly submitted claims 11-16 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are directed to SEQ ID NO:1074. This is a previously non-elected polypeptide (see Paper No. 10, mailed 8-28-01).

Since applicant has received an action on the merits for the originally presented invention (SEQ ID NO:1047), this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-16 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. This application contains claims 11-16 drawn to an invention nonelected with traverse in Paper No. 9, mailed June 4, 2001. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

New Rejections Based on Amendment

5. Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As to claim 17, Markush member (ii), and claims 18-22 as depending from such, the specification as originally filed fails to provide conception for the invention as is now claimed, as polypeptides encoded by hybridizing polynucleic acids. This issue is best resolved by Applicants pointing to the specification by specific page and line number where conception by way of written description for the now claimed embodiment can be found.

6. Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification broadly describes as part of the invention isolated polynucleotides comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:1047 that has an

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alleged function as a "tryptophan hydroxylase" (see page 4, fifth full paragraph and Table 2, page 51). The specification also broadly describes the tryptophan hydroxylase polypeptide specifically, by reference to the polynucleotide sequence of SEQ ID NO:1047.

The claims encompass polypeptide sequences comprising SEQ ID NO:1047, comprising sequences that have a recited degree of identity as compared to the polypeptide sequence of SEQ ID NO:1047, and polypeptide sequences encoded by a nucleic acid sequence that hybridizes to residues 1200537-1201343 of SEQ ID NO: 1 which have no associated function. These isolated polypeptide variants correspond to sequences from other bacterial species, mutated sequences and allelic variants. None of these sequences meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification only discloses a polypeptide comprising SEQ ID NO: 1047 which corresponds to the polynucleic acid sequence encoding the *Chlamydia pneumoniae* species of the protein "tryptophan hydroxylase" comprising the amino acid sequence set forth in SEQ ID NO:1047, which corresponds to the polynucleic acid sequence of a fragment of the genomic DNA of the *Chlamydia pneumoniae* species of the protein. The specification provides no written description of any variants of the polypeptide, nor does it describe any variants of the polynucleotide that encode such variants of the polypeptide that hybridize as claimed. Thus, only an isolated polypeptide sequence comprising the amino acid sequence set forth in SEQ ID NO:1047 meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The specification has not described nor disclosed any variants of the protein sequence or any variants of the polynucleotide sequence encoding variants of the polypeptide sequence. One skilled in the art would recognize that the Applicant was not apparently in possession of the claimed percent identical proteins or hybridizing variants of the protein. The specification fails to teach a single variant of a polypeptide sequence of SEQ ID NO:1047 and it is noted that the claimed polynucleotides do not exist as an invention independent of their function in encoding a tryptophan hydroxylase. The actual structure or other relevant identifying characteristics of each nucleic acid that encodes a variant protein having the properties of the disclosed tryptophan hydroxylase protein can only be determined empirically by actually making every nucleic acid that encodes the recited variability (i.e. the substitutions, insertions or deletions as compared to SEQ ID NO:1) and testing each to determine whether it encodes a protein having the particularly

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disclosed properties of an riboflavin synthase (alpha-subunit) enzyme. As noted in the Guidelines at Section I.A.(2):

There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The specification proposes the converse, yet still does not meet the requirements for an adequate written description of the claimed invention. The specification proposes that the skilled artisan is to modify a known nucleic acid sequence encoding a known protein sequence and that modification would still describe applicant's invention as a *Chlamydia pneumoniae* tryptophan hydroxylase as disclosed. The tryptophan hydroxylase, disclosed as SEQ ID NO:1047, is a putative member of the tryptophan hydroxylase family of enzymes and has specific biological properties dictated by the structure of the protein and the corresponding structure of the structural nucleotide sequence which encodes it. There must be some nexus between the structure of a nucleotide sequence, the structure of the protein encoded, and the function of that encoded protein. However, function can not be predicted from the modification of the structure of the gene sequence or in this case the nucleotide sequence encoding the protein. The specification has not shown that, by modifying a reference sequence encoding a reference polypeptide as claimed, will automatically predict the production of a tryptophan hydroxylase as disclosed. While it is true that, due to the nature of codon degeneracy, applicant may take a reference sequence and modify that sequence to be a different nucleic acid sequence, yet still have that nucleic acid encode the same tryptophan hydroxylase protein. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of a representative number of polynucleotides encoding a representative number of tryptophan hydroxylase polypeptides, or a representative number of polypeptide variants sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. With the exception of an isolated polypeptide comprising the amino acid sequence as set forth in SEQ ID NO:1047, the skilled artisan cannot envision the contemplated polypeptide sequences by the detailed chemical structure of the claimed polynucleotides because the genus is so highly variant and therefore conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. The specification fails to provide a representative number of protein or nucleic acid variants encoding such, to indicate that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the single disclosed species of SEQ ID NO:1047.

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Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 1047 and associated compositions, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (See page 1115.)

7. Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:1047 and associated compositions, the specification does not reasonably provide enablement for 80% identical variants of SEQ ID NO:1047, or polypeptides encoded by nucleic acid sequences that hybridize to a sequence consisting of residues 1200537-1201343 of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to and encompass polypeptides variants that have 80% identity variants of SEQ ID NO:1047, or polypeptides variants that are encoded by nucleic acid sequences that hybridize to a sequence consisting of residues 1200537-1201343 of SEQ ID NO:1. These claims are not enabled for the following reasons. The written description is limited to a single complete open reading frame consisting of SEQ ID NO:1047 which is the corresponding amino acid sequence encoded by the polynucleotide consisting residues 1200537-1201343 of SEQ ID NO:1. The specification fails to indicate that SEQ ID NO:1047 has the biological activity of a tryptophan hydroxylase and further lacks any description of any variants of either the polypeptide or the corresponding polynucleotide sequence which act as a tryptophan hydroxylase. The specification provides no evidence that SEQ ID NO:1047 has the appropriate enzymatic activity. The specification is also not enabled for the claimed variants of a polypeptide, because 1) the specification fails to teach where and how much variation of SEQ ID NO:1047 is permitted such that the polynucleotide sequence or protein sequence encoded thereby is still able to function in any particular means described in the specification: diagnostic, protective vaccine or as a tryptophan hydroxylase; 2) the specification lacks any written description of any variants of SEQ ID NO:1047 or any hybridizing variants of the polynucleotide sequence that encode polypeptides as claimed which are capable of functioning as a

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diagnostic as asserted in the specification and specific assay conditions, such as substrate, pH, temperature etc., which could be used to determine working diagnostic/protective embodiments within the scope of hybridizing polynucleotides encoding polypeptides or polypeptide variants; 3) the specification fails to teach how to use nucleic acid sequences which are hybridizing variants of SEQ ID NO:1 residues 1200537-1201343, in diagnosis or detection because the specification fails to teach what are the critical nucleic acid residues that can be modified and still achieve a nucleic acid that will function as a diagnostic or detection reagent or vaccine reagent for *Chlamydia pneumoniae*; 5) the art teaches that polynucleotides isolated based on percent homology do not predictably display the functions of their homologs and one skilled in the art would have reason to doubt the assertion that SEQ ID NO:1047 has the ability to act as a tryptophan hydroxylase; 6) the art teaches that even replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition of a protein, one skilled in the art would have reason to doubt the validity and functionality of the asserted enzymatic function of the protein of SEQ ID NO:1047 and the detection or diagnostic use of variants thereof, and the detection or diagnostic use of variants of isolated nucleic acids encoding variants of the protein of SEQ ID NO:1047, and 7) the specification has not displayed a nexus between the structure of the nucleotide sequence and function of the protein as either a protein with tryptophan hydroxylase activity or a protein variant with detection or diagnostic use.

As to points 1)- 7), the specification fails to provide a written description of any protein variants (i.e. the mature form, prepro form, the pro form, species variants) of the protein sequence of SEQ ID NO:1047, and the corresponding encoding polynucleic acids, which function equivalently to a polypeptide comprising the disclosed SEQ ID NO:1047 or are able to be used as a diagnostic or detection or vaccine reagent as contemplated in the specification. The specification fails to teach the critical protein residues involved in the function of the protein SEQ ID NO:1047 or that SEQ ID NO:1047 has the ability to function as a tryptophan hydroxylase, such that the skilled artisan is provided no guidance to test, screen or make nucleic acid sequence variants of the polynucleic acids encoding the variants of the polypeptide of comprising SEQ ID NO:1047 or the polynucleotide comprising SEQ ID NO:1047, using conventional technology which allow for a screening or generic diagnostic or vaccine use asserted in the specification. The specification fails to teach to what extent you could alter SEQ ID NO:1047 and still present the sequence as diagnostic. The specification utterly fails to teach that the isolated protein provides for a composition that is protective from infection (i.e. vaccine) and the art does not recognize the genus of tryptophan hydroxylase enzymes as possessing such activity. One skilled in the vaccine art would have substantial reason to doubt that the protein of SEQ ID NO:1047 could be used as a vaccine as asserted in the specification. As such, screening

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for variants that are protective would be a futile endeavor unless one skilled in the art had *a priori* knowledge that the parent molecule exhibited the desired activity. In order to be diagnostic the sequence must distinguish *Chlamydia pneumoniae* from other pathogenic bacterial species, other Chlamydial sp. and other clinically relevant autochthonous bacteria in a host. The specification also fails to demonstrate the actual biological function of the DNA and protein and only speculates on the protein's function based on fractional homology to other sequences. One skilled in the art would have reason to doubt the alleged function of the protein and polynucleic acid encoding the protein because the specification fails to teach that the protein produced by the DNA actually functions as asserted and the art teaches that polynucleotides isolated based on percent homology do not predictably display the functions of their homologs. Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Gerhold et al.[BioEssays, Volume 18, Number 12, pages 973-981(1996)]; Wells et al.[Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550 (1997)]; and Russell et al.[Journal of Molecular Biology, Volume 244, pages 332-350 (1994)]. Even if one were to demonstrate that SEQ ID NO:1047 functioned as tryptophan hydroxylase the specification is not enabled for polynucleotides encoding protein variants because the specification fails to teach the appropriate substrate and assay which one skilled in the art could use to screen for polynucleic acids encoding variants of SEQ ID NO:1047 which are encompassed by the claimed variation of SEQ ID NO:1047. The art establishes that enzymes from different sources differ in their regulatory mechanisms and in their natural substrates. No substrate assay for function or guidance for setting forth parameters of a functional assay is set forth in the specification which would allow one skilled in the art to screen for biologically functionally equivalent variants of either the protein or diagnostic use of encoding polynucleotides or variants of SEQ ID NO:1047 for specific detection and the specification does not

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specifically point to a particular one in the art would could be relied upon for screening for polypeptides and polynucleotides encoding them for diagnostic or screening use. One of skill in the art would be reduced to merely randomly altering nucleic acids which would lead to unpredictable results regarding the functional activity of the nucleic acid and the ability of the nucleic acid to be used as a diagnostic reagent, detection reagent or encode a functional protein and one skilled in the art would be unable to test for functionality of the polypeptide variants of SEQ ID NO:1047. Thus, one skilled in the art could not even screen for working embodiments within the scope of the claim because no assay is set forth in the specification. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted *a priori* and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3):1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of a single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol., 1991, 5(7):1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. The specification has not taught which residues of SEQ ID NO:1047 can be varied and still achieve a protein that is functional as a tryptophan hydroxylase or is capable of use as a diagnostic using immunological means of recognition. The specification has not conceived any other functionally equivalent protein variant or the polynucleic acid sequence encoding the protein variant does not set forth the general tolerance to substitutions, where substitutions could be made and how to assay for these variants. Since, the specification lacks a written description of any variant comprising the sequence of SEQ ID NO:1 or a protein sequence of SEQ ID NO:1047 which has the ability to

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function as a tryptophan hydroxylase as alleged, it is not enabled for this variant language because it fails to enable the skilled artisan to envision the detailed chemical structure of the claimed protein variants of SEQ ID NO:1047 or that SEQ ID NO:1047 functions as alleged, respectively, as well as the screening method of obtaining them, as well as how to use the polynucleotides encoding the protein variants, one of skill in the art would be unable to produce these polynucleotides encoding protein variants, produce a biologically active protein or polynucleotide variants encompassed by the instant claims. The art of record teaches that polynucleotides isolated based on percent homology do not predictably display the functions of their homologs absent some independent teaching that the sequence produces a protein that functions as alleged. Thus, biological function ascribed the gene product based on solely structural or sequence identity is unreliable and unpredictable in the absence of supporting production of the protein and functional analysis. There is no evidentiary support that the instant protein has use and functions as a tryptophan hydroxylase. Moreover, from the definition of Applicants' invention as set forth in the specification, it is unclear exactly what the composition of any tryptophan hydroxylase will be if it is expressed by a nucleic acid which has the claimed changes. For, example, if one nucleotide is deleted or inserted at a single place within the coding sequence, all the codons down stream of that insertion or deletion will be frame shifted. If that frame shift takes place near the 5' end of the gene, it is highly likely that the protein expressed will have little in common structurally or functionally with the tryptophan hydroxylase. The teachings of the specification fail to allow one skilled in the art to predict what effect a given change in the hybridizing nucleic acid sequence will cause in the protein sequence. Such changes are not enabled as applicants' invention, which is disclosed as a detection reagent or tryptophan hydroxylase. In this regard, applicant has not enabled the scope of the invention as claimed for those nucleic acids encoding a SEQ ID NO:1047 variant that would be altered, as now claimed. The specification discloses a putative tryptophan hydroxylase and a nucleic acid encoding it. The protein has specific immunological and biological properties which are the result of its primary acid sequence as encoded by this nucleic acid sequence. Applicants' proposed insertions, deletions or substitutions to that nucleic acid sequence do not predict a protein having all the identifiable properties of the tryptophan hydroxylase as disclosed. Therefore, such undisclosed and unidentified nucleic acids which result from these, insertions, deletions or substitutions encompassed by the recited "insertions, deletions or substitutions" are not enabled for their scope. The skilled artisan would be forced into undue experimentation to make and use the instantly claimed scope of invention. Although the skilled artisan might envision making a great number of changes of a reference nucleic acid sequence or a polypeptide in accordance with applicant's disclosure, it is unclear exactly that the protein which is expressed therefrom would be the tryptophan hydroxylase disclosed as applicants'

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invention or that these altered nucleic acids would diagnose or detect the presence of *Chlamydia pneumoniae*. These altered nucleic acids would encode a polypeptide which would vary from the disclosed tryptophan hydroxylase amino acid sequence in some unknown or unpredictable manner. *Amgen Inc. v. Chugai Pharmaceutical Co. Inc.* 18 USPQ2d 1016, 1026 (CAFC 1991) addressed a similar issue of enablement and undue experimentation for analogs of erythropoietin (EPO) gene broadly claimed and narrowly disclosed. In that instance, it was found:

that over 3,600 different EPO analogs can be made by substituting at only a single amino acid position, and over a million different analogs can be made by substitution three amino acids. The patent indicates that it embraces means for preparation of "numerous" polypeptide analogs of EPO. Thus, the number of claimed DNA sequences encoding sequences that can produce EPO-like product is potentially enormous.

Further, at page 1027, the CAFC found that:

it is not necessary that a patent applicant test all the embodiments of his invention, ... what is necessary is that he provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. For DNA sequences, this means disclosing how to make and use enough sequence to justify a grant of the claims sought. Amgen has not done that here. In addition, it is not necessary that a court review all of the *Wands* factors to find a disclosure enabling. They are not illustrative, not mandatory. What is relevant depends on the facts, and the facts here are that Amgen has not enabled preparation of DNA sequences to support its all-encompassing claims... Here, however, despite extensive statements in the specification concerning all the analogs of the EPO gene that can be made, there is little enabling disclosure of particular analogs and how to make them. Details for preparing only a few EPO analogs genes are disclosed. Amgen argue that this is sufficient to support its claims; we disagree. This "disclosure" might well justify a generic claim encompassing these and similar analogs, but it represents inadequate support for Amgen's desire to claim all EPO analogs. There may be other genetic sequence that code for EPO-Type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them...[W]e do not intend to imply that genetic sequences cannot be valid where they are of a scope appropriate to the invention disclosed by an applicant. That is not the case here, where Amgen has claimed every possible analog of a gene containing about 4,000 nucleotides, with a disclosure of how to make EPO and a very few analogs.

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Finally, at page 1028, the CAFC concludes:

Considering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with an attendant uncertainty as to what utility will be possessed by these analogs, we consider that more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity. It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity. Under the circumstances, we find no error in the court's conclusion that generic DNA sequence claims are invalid under section 112.

See also *In re Due*/ 34 USPQ2d 1210 (CAFC 1995); *Colbert v. Lofdahl* 21 USPQ2d 1068 (Bd. Pat. Ap. Inter. 1991); and *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997).

In view of the lack of written description of any protein or protein variant of SEQ ID NO:1047 that functions equivalently to the tryptophan hydroxylase of the art as alleged and the corresponding nucleic acid sequence, the lack of enabling description of make and use polynucleotides variants of SEQ ID NO:1, the lack of enabling description of make and use polypeptides encoded by polynucleotide variants of SEQ ID NO:1, the lack of an enabling written description of how to obtain and make and use the nucleic acid variants of the of the polynucleotide sequence of SEQ ID NO:1, the unpredictability associated with making and using the polypeptides encoded by the nucleic acids encoding the myriad variants of SEQ ID NO:1 encompassed in the scope of the claims as set forth above, the lack of teaching even a beginning point for variation of the nucleic acid for routine experimentation, the lack of an assay to screen for variants, lack of working examples commensurate in scope with the instant claims, that one skilled in the art has substantial reason to doubt that SEQ ID NO:1047 has the biological activity of a tryptophan hydroxylase, the skilled artisan would be forced into undue experimentation to practice (i.e. make and use) the invention as is broadly claimed.

Claim Rejections - 35 U.S.C. § 102 and 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. No support for SEQ ID NO:1047 is apparently found in the priority document(s). This issue is best resolved by Applicants pointing to the priority document by specific page and line number where specific contemplation and written description support for SEQ ID NO:1047 is found in the priority document(s).

11. Claim 17 is rejected under 35 U.S.C. 102(a) as being clearly anticipated by PIR_68 Database Accession Number E72002, dated 23 April 1999.

Accession Number E72002 teaches a polypeptide that has 99.8% identity with the polypeptide of SEQ ID NO:1047. As such, this reference anticipates Markush member (I) of claim 17.

12. Claim 17 is rejected under 35 U.S.C. 102(a) as being clearly anticipated by Griffais, R (WO 99/27105, published 03 June 1999) as represented by Genseq_0601 Database Accession Number AAY35703 attached hereto.

Griffais teaches a polypeptide from *Chlamydia pneumoniae* that has 91.8 % similarity and 66.2 % identity with SEQ ID NO:1047 and is 100% identical across greater than 200 consecutive amino acids (see attached alignment). The polynucleotide encoding this highly similar protein as taught by Griffais (see attached alignment) would hybridize

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with residues 1200537 to 1201343 of SEQ ID NO:1. Griffais contemplates polypeptides encoded by a polynucleotide sequence that hybridizes to SEQ ID NO:1 or an open reading frame thereof (see page 14, first full paragraph). As such, this reference meets the limitation of Markush member (ii) of claim 17. Further, Griffais teaches the isolated polypeptide in a composition comprising a pharmaceutically acceptable carrier or an adjuvant (see page 68, lines 25-35, page 70, lines 32-35). Griffais teaches the attachment of polypeptides to a chip (i.e. the instant solid phase; see page 283, Claim 31). Griffais et al also teach that the polypeptides of the invention may be use in a method of detection or the identification of bacteria belonging to the species of *Chlamydia pneumoniae* (see page 59, first full paragraph). Griffais also teaches that the protein may be any conventional procedure for the detection of any antigen/antibody complexes that may be formed such as, ELISA and deposition of the protein on the microtiter plate (i.e. solid surface). These teachings anticipate claims 18-21.

13. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Griffais, R (WO 99/27105, published 03 June 1999) as represented by Genseq_0601 Database Accession Number AAY35703 in view of Catty et al (Antibodies, Vol II, A Practical Approach, IRL Press at Oxford University Press 1989, pages 97-154.

Griffais is set forth *supra*. Griffais differs by not attaching the protein of interest to nitrocellulose.

Catty et al teaches that a variety of solid phase surfaces have been exploited for ELISA assays, including nitrocellulose (see page 97, last line of first paragraph).

It would have been *prima facie* obvious to substitute the nitrocellulose solid phase for the microtiter plate solid phase of Griffais because Griffais teaches that the protein of interest can be used in any procedure for the detection of antigen/antibody complexes such as ELISA and Catty et al teach that nitrocellulose is a conventional solid phase carrier for dot-ELISA assays.

14. Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffais, R (WO 99/27105, published 03 June 1999) as represented by Genseq_0601 Database Accession Number AAY35703 in view of PIR_68 Database Accession Number E72002, dated 23 April 1999.

Griffais is set forth *supra*. Griffais differs by not teaching a protein that has 80% identity with SEQ ID NO:1047.

PIR_68 Database Accession Number E72002, dated 23 April 1999 teaches a polypeptide from *Chlamydia pneumoniae* that is 99.8% identical with SEQ ID NO:1047.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to substitute the protein of PIR_68 Database Accession

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Number E72002 from *Chlamydia pneumoniae* for any of the *Chlamydia pneumoniae* polypeptides and compositions of Griffais because Griffais teaches the polypeptides are useful in detection of infection and making antibodies for detection of the *Chlamydia pneumoniae* microorganism.

15. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Griffais, R (WO 99/27105, published 03 June 1999) as represented by Genseq_0601 Database Accession Number AAY35703 in view of PIR_68 Database Accession Number E72002, dated 23 April 1999 as applied to claims 18-21 *supra*, further in view of Catty et al (Antibodies, Vol II, A Practical Approach, IRL Press at Oxford University Press 1989, pages 97-154.

Griffais and PIR_68 Database Accession Number E72002 are set forth *supra*. The compositions as combined differ by not teaching nitrocellulose as a solid phase.

Catty et al teaches that a variety of solid phase surfaces have been exploited for ELISA assays, including nitrocellulose (see page 97, last line of first paragraph).

It would have been *prima facie* obvious to substitute the nitrocellulose solid phase for the microtiter plate solid phase of Griffais and PIR-68 Accession Number E72002 as combined *supra* because Griffais teaches that the protein of interest can be used in any procedure for the detection of antigen/antibody complexes such as ELISA and Catty et al teach that nitrocellulose is a conventional solid phase carrier for dot-ELISA assays.

Status of Claims

16. All claims stand rejected or withdrawn from consideration.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

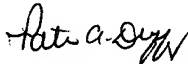
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18. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Thursday and Saturday from 10:30 AM to 7:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
May 18, 2002


Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600